UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/733,135	12/11/2003	Charles Joel Arntzen	P00245US17	8272

22885 7590 01/18/2007

MCKEE, VOORHEES & SEASE, P.L.C.
801 GRAND AVENUE
SUITE 3200
DES MOINES, IA 50309-2721

EXAMINER	
WORLEY, CATHY KINGDON	
ART UNIT	**PAPER NUMBER**
1638	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/733,135	ARNTZEN ET AL.	
	Examiner	Art Unit	
	Cathy K. Worley	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *11-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 May 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/11/03; 1/18/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Restriction/Election

1. In response to the communication received on Oct. 24, 2006 from Heidi S. Nebel, the election with traverse of group I, claims 1-10, is acknowledged. The Applicant did not provide any grounds for the traversal, therefore the restriction requirement is maintained. Because applicant did not distinctly and specifically point out any errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The restriction requirement is made FINAL.

Claims 1-14 are pending, and claims 11-14 are withdrawn from consideration for being drawn to a non-elected invention.

Claims 1-10 will are examined in the present office action.

Oath/Declaration

2. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP 602.01 and 602.02.

The oath has a box checked identifying this application as a continuation-in-part (CIP), and therefore a new oath signed by both inventors is required.

Specification

3. The specification is objected to because there are sequences on page 39, in lines 17 and 18 that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825. The specification needs to be amended to include the sequence identifiers for each of these sequences.

4. The specification is objected to because the drawings are not referred to properly. If the drawings show Figures 7A and 7B; or Figures 10A and 10B, then the Brief Description of the Drawings should recite "Figures 7A-7B", instead of "Figure 7" and "Figures 10A-10B, instead of "Figure 10". Correction is requested.

5. The use of the following trademarks has been noted in this application: TWEEN, ZYMED, AFFI-GEL, BIO-RAD, and LAB-TEK. They should be written in all capital letters wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Information Disclosure Statement

6. The information disclosure statement filed Dec. 11, 2003, fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

7. The listing of references in the specification on pages 50-51 is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Drawings

8. The drawings are objected to because Figure 2 and Figure 5 appear on the same page, with Figures 3 and 4 following. Therefore, the Figures are not in proper order. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Objections

9. Claim 1 is objected to because of the following informalities: Claim 1 recites "transforming a plant with a nucleotide construct expressing a recombinant viral immunogen in a plant". It is unclear how a plant can be transformed with a construct that is already expressing in a plant. Replacing "expressing" and with - - that expresses - - will obviate this objection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. All dependent claims are included in these rejections.

Claims 1, 8, and 9 recite "a nucleotide construct", and it is unclear how a single nucleotide can comprise a construct. Replacing "nucleotide" with - - nucleic acid - - will obviate this rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 1-5 and 7-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goodman et al. (US Patent No. 4,956,282, issued on Sept. 11, 1990) in view of Kapikian et al. (Reviews of Infectious Diseases (1989) Vol. 11, supplement 3, pp. S539-S546).

The claims are drawn to a method of producing an immunogenic composition, wherein said method comprises the steps of transforming a plant with a nucleic acid encoding a recombinant viral immunogen, and producing from said plants said composition. Claim 1 includes "selecting those plants expressing said recombinant viral immunogen at a level such that upon oral administration of a composition comprising a plant-expressed recombinant viral immunogen to an animal, an immunogenic response to said viral immunogen is elicited". The office interprets this recitation to be inclusive of any expression level because the composition can comprise recombinant viral immunogen that has been purified and/or concentrated; therefore the amount of immunogen in the composition is not related to the level of expression in the plant. Therefore, this part of the claim is not considered a further

limitation. Claims 4, 8, and 9 contain similar language and are therefore inclusive of plants with any expression level.

Goodman et al. teach the production of recombinant proteins in plants, including proteins encoded by mammalian viral pathogen genes (see column 3, lines 11-13). They suggest that antigens associated with viral pathogens could be expressed (see column 3, lines 31-32). Antigens are also referred to in the art as immunogens (see page 9 of the instant specification, line 2). They teach that in some instances the recombinant protein can have a physiological effect on ingestion, and it will be sufficient for the product to be retained in an edible plant part (see column 5, lines 51-56). They teach that plants that can be employed for the production of recombinant proteins may be either monocots or dicots (see column 4, lines 55-56), that the DNA construct can be transferred into the plant cell by *A. tumefaciens*, or *A. rhizogenes*, microinjection, liposome fusion, or viral infection (see column 4, lines 43-45) which are all means of transforming a plant with a construct. Goodman et al. teach transcriptional initiation regions (also referred to as promoters), including the napin promoter for expression in seeds (which is an edible tissue of a plant) (see column 2, lines 43-58). They suggest the used of several different species of plants that are edible by an animal, including sunflower, corn, sugar cane, soybean, tomato, alfalfa, mustard, and sugar beet (see column 4, lines 59-60).

Goodman et al. do not teach an immunogen from a transmissible gastroenteritis virus, nor do they teach an immunogen that is capable of generating an immunogenic response when it interacts with a mucosal membrane.

Kapikian et al. teach an immunogen from a transmissible gastroenteritis virus that is capable of generating an immunogenic response when it interacts with a mucosal membrane, (see pages S542-S543 for a discussion of candidate vaccines, and see page S542, right column, last paragraph, where is states that the vaccine was shown to be safe and antigenic after oral administration which shows that is generates an immunogenic response when it interacts with a mucosal membrane).

Given the recognition of those of ordinary skill in the art of the value of expressing an immunogenic protein in a plant as taught by Goodman et al. (see column 3, lines 31-32), it would have been obvious to one of ordinary skill in the art to use the method of Goodman et al. and to modify said method using the sequences encoding the immunogens taught by Kapikian et al. One would have been motivated to express the immunogens taught by Kapikian et al. because they teach that it is important to find a safe, inexpensive, and effective rotavirus vaccine (see page S539, left column, first paragraph) because such a vaccine can prevent diarrheal diseases that cause about 12, 600 deaths per day (see page S539, paragraph bridging left and right columns). Furthermore Kipikian et al. specifically state that an orally administered vaccine would be the most effective (see page S541, left column, first paragraph) and Goodman et al. specifically suggest

that their method can be utilized to grow recombinant viral antigens (see column 3, lines 31-35) and they teach that it could be used for expression in an edible plant part for proteins that can have a physiological effect on ingestion (see column 5, lines 51-56). Given the success of producing recombinant therapeutic proteins in plants taught by Goodman et al. and the success of utilizing recombinant proteins for vaccines as taught by Kapikian et al., one would expect success in combining the teachings.

Thus, the claimed invention would have been *prime facie* obvious as a whole to one of ordinary skill in the art at the time it was made, especially in the absence of evidence to the contrary.

12. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Goodman et al. (US Patent No. 4,956,282, issued on Sept. 11, 1990) in view of Kapikian et al. (Reviews of Infectious Diseases (1989) Vol. 11, supplement 3, pp. S539-S546), as applied to claims 1-5 and 7-10 above, and further in view of Kay et al. (Science (1987), Vol. 236, pp. 1299-1302), and further in view of Gallie et al. (MGG (1991), Vol. 228, pp. 258-264).

The claims are drawn to a method of producing an immunogenic composition, wherein said method comprises the steps of transforming a plant with a nucleic acid encoding a recombinant viral immunogen and comprising a 5' untranslated leader sequence and an enhancer; and producing from said plants said composition.

Goodman et al. in view of Kapikian et al. have been discussed above.

Goodman et al. in view of Kapikian et al. do not teach the use of a 5' untranslated leader sequence, nor do they teach an enhancer sequence.

Kay et al. teach the use of an enhancer from the CaMV 35S upstream sequences (see page 1299, middle column).

Gallie et al. teach the use of a 5' untranslated leader sequence (see page 258, right column).

Given the recognition of those of ordinary skill in the art of the value of utilizing and enhancer as taught by Kay et al. and a 5' untranslated leader sequence as taught by Gallie et al., it would have been obvious to one of ordinary skill in the art to use the method of Goodman et al. and to modify said method by using the enhancer taught by Kay et al. and the 5' untranslated leader sequence taught by Gallie et al and by expressing the immunogens taught by Kapikian et al.

One would have been motivated to utilize an enhancer because Kay et al. teach that the presence of the enhancer leads to 40-fold higher levels of expression of a transgene (see page 1301, left column, first paragraph).

One would have been motivated to use a leader sequence because Gallie et al. teach that a leader sequence substantially enhances translation of a gene construct (see page 258, right column, second paragraph).

One would have been motivated to express the immunogens taught by Kapikian et al. because they teach that it is important to find a safe, inexpensive,

and effective rotavirus vaccine (see page S539, left column, first paragraph) because such a vaccine can prevent diarrheal diseases that cause about 12, 600 deaths per day (see page S539, paragraph bridging left and right columns).

Given the successes taught in the prior art, one would expect to succeed in expressing a recombinant viral immunogen utilizing a nucleic acid construct comprising a leader sequence and an enhancer in the method taught by Goodman et al.

Thus, the claimed invention would have been *prime facie* obvious as a whole to one of ordinary skill in the art at the time it was made, especially in the absence of evidence to the contrary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 1-10 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 5-6 and 9-14 of U.S. Patent No. 5,484,719, issued on Jan. 16, 1996.

The instant claims are drawn to a method of producing an immunogenic composition, wherein said method comprises the steps of transforming a plant with a nucleic acid encoding a recombinant viral immunogen, and producing from said plants said composition.

Claims 5-6 and 9-14 of U.S. Patent No. 5,484,719 are drawn to a method for constructing a transgenic tobacco plant expressing a hepatitis B viral surface antigen.

Although the conflicting claims are not identical, they are not patentably distinct from each other.

Claim 1 of the instant application encompasses methods of producing any viral immunogen in a plant; therefore, claims 5-6 of U.S. Patent No. 5,484,719 encompass a species of the genus encompassed by the instant claims (ie. hepatitis B is one viral immunogen). Because a species anticipates the genus, claims 5-6 and 9-14 of U.S. Patent No. 5,484,719 anticipate claim 1 of the instant application.

The remaining limitations in the instant claims 2-10 that do not appear in the issued patent are obvious in view of the prior art.

14. Claims 1-10 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 2-14 of U.S. Patent No. 5,612,487, issued on Mar. 18, 1997.

The instant claims are drawn to a method of producing an immunogenic composition, wherein said method comprises the steps of transforming a plant with a nucleic acid encoding a recombinant viral immunogen, and producing from said plants said composition.

Claims 2-14 of U.S. Patent No. 5,612,487 are drawn to a method for producing an antigenic composition comprising making a transgenic tobacco plant expressing a hepatitis B viral surface antigen.

Although the conflicting claims are not identical, they are not patentably distinct from each other.

Claim 1 of the instant application encompasses methods of producing any viral immunogen in a plant; therefore, claims 2-14 of U.S. Patent No. 5,612,487 encompass a species of the genus encompassed by the instant claims (ie. hepatitis B is one viral immunogen). Because a species anticipates the genus, claims 2-14 of U.S. Patent No. 5,612,487 anticipate claim 1 of the instant application.

The remaining limitations in the instant claims 2-10 that do not appear in the issued patent are obvious in view of the prior art.

15. Claims 1-10 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 14 of U.S. Patent No. 5,792,935, issued on Aug. 11, 1998.

The instant claims are drawn to a method of producing an immunogenic composition, wherein said method comprises the steps of transforming a plant with a nucleic acid encoding a recombinant viral immunogen, and producing from said plants said composition.

Claims 14 of U.S. Patent No. 5,792,935 is drawn to a method for producing a transgenic Musa plant expressing a pharmaceutical protein, including the hepatitis B surface antigen and the Norwalk virus capsid protein.

Although the conflicting claims are not identical, they are not patentably distinct from each other.

Claims 1 and 3 of the instant application encompasses methods of producing any viral immunogen in any plant, or of producing an immunogen from any transmissible gastroenteritis virus in any plant; therefore, claim 14 of U.S. Patent No. 5,792,935 encompasses a species of the genus encompassed by the instant claims (ie. hepatitis B is one viral immunogen and Norwalk capsid protein is an immunogen from one transmissible gastroenteritis virus; and a Musa plant is one kind of plant). Because a species anticipates the genus, claim 14 of U.S. Patent No. 5,792,935 anticipates claims 1 and 3 of the instant application.

The remaining limitations in the instant claims 2 and 4-10 that do not appear in the issued patent are obvious in view of the prior art.

16. Claims 1-10 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 8-11 of U.S. Patent No. 6,034,298, issued on Mar. 7, 2000.

The instant claims are drawn to a method of producing an immunogenic composition, wherein said method comprises the steps of transforming a plant with a nucleic acid encoding a recombinant viral immunogen, and producing from said plants said composition.

Claims 8-11 of U.S. Patent No. 6,034,298 are drawn to a method for constructing a transgenic plant expressing an immunogen from any transmissible gastroenteritis virus.

Although the conflicting claims are not identical, they are not patentably distinct from each other.

Claims 1 and 3 of the instant application encompasses methods of producing any viral immunogen in any plant, or of producing an immunogen from any transmissible gastroenteritis virus in any plant; therefore, claims 8-11 of U.S. Patent No. 6,034,298 encompass a species of the genus encompassed by the instant claims (ie. a viral immunogen from a transmissible gastroenteritis virus is one viral

immunogen). Because a species anticipates the genus, claims 8-11 of U.S. Patent No. 6,034,298 anticipate claims 1 and 3 of the instant application.

The remaining limitations in the instant claims 2 and 4-10 that do not appear in the issued patent are obvious in view of the prior art.

17. No claims are allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cathy K. Worley whose telephone number is (571) 272-8784. The examiner is on a variable schedule but can normally be reached on M-F 10:00 - 4:00 with additional variable hours before 10:00 and after 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CKW

STUART F. BAUM, PH.D
PRIMARY EXAMINER